REMARKS

This is meant to be a complete response to the Office Action mailed August 16, 2002. In the Office Action, the Examiner rejected Applicants' claims 22, 23, 32-41 and 43-47 under 35 U.S.C. 112, ¶2 and claims 19, 21-23, 25-27, 32-41 and 43-47 under 35 U.S.C. 112, ¶1. Such claims have been canceled herein, without prejudice, and therefore Applicants respectfully submit that the 35 U.S.C. 112, ¶1 and ¶2 rejections of the claims has been rendered moot.

In addition, the Examiner rejected Applicants' claims 19-27 and 41-47 under 35 U.S.C. 102(a) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over McCourt et al., Hepatology 30:1276, or Zhou et al., JBC 274(48):33831-33834. Further, the Examiner rejected Applicants' claims 19-27 and 41-47 under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Yannariello-Brown et al., Glycobiology 7:15. Claims 19-23, 25-27, 29-41 and 43-47 have been canceled herein, and therefore Applicants respectfully submit that the rejections of such claims have been rendered moot.

Claims 24, 28, 42 and 88 are pending in this application, with claim 28 currently withdrawn from consideration as being drawn to a non-elected species. Claims 24 and 28, as amended, and newly added claim 88, recite a purified mammalian HARE comprising a protein which is able to specifically bind at least one of HA, chondroitin and chondroitin sulfate, wherein the protein comprises a sequence **essentially as set forth in** SEQ ID NO:2 or SEQ ID

NO:25. Claim 42, as amended, recites a purified composition comprising a functionally active HARE polypeptide having an amino acid sequence selected from the group consisting of an amino acid sequence **essentially as set forth in** SEQ ID NO:2 and an amino acid sequence **essentially as set forth in** SEQ ID NO:25.

Support for the amendments to the claims can be found in Paragraphs **[0068] - [0071]** and Table I of the Specification. Therefore, Applicants respectfully submit that claims 24, 28, 42 and 88 are definite and particularly point out and distinctly claim that which Applicants regard as the invention; that such claims reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention; and that such claims enable a person having ordinary skill in the art to make and use the invention.

Applicants' Response to the 35 U.S.C. 102(a)/103(a) Rejection of the Claims

In the Office Action, the Examiner rejected Applicants' claims 19-27 and 41-47 under 35 U.S.C. 102(a) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over McCourt et al., Hepatology 30:1276, or Zhou et al., JBC 274(48):33831-33834.

Applicants respectfully traverse the rejection of pending claims 24 and 42 based on the 37 CFR 1.132 declaration attached hereto. The declaration, signed by co-Applicant Paul Weigel, establishes that the Zhou et al. paper

describes the Applicants' own work. The declaration also establishes that the differences in inventorship of the subject application and authorship of the Zhou et al. paper are two-fold: (1) Janet Oka and Janet Weigel are the same person, the "Oka" being Janet Weigel's maiden surname; and (2) Anil Singh is a laboratory technician who merely worked under the direction of the Applicants and did not contribute to the conception of the present invention. Therefore, Applicants respectfully submit that Zhou et al. is not a proper reference under 35 U.S.C. 102(a)/103(a).

In addition, McCourt et al. was accepted for publication on August 9, 1999, and therefore the actual publication date of this reference would have to be after August 9, 1999. The Zhou et al. reference was received for publication on July 25, 1999, thereby demonstrating conception and constructive reduction to practice of the present invention prior to the publication date of the McCourt et al. reference. Therefore, Applicants respectfully submit that McCourt et al. is also not a proper reference under 35 U.S.C. 102(a)/103(a).

Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. 102(a)/103(a) rejection of pending claims 24 and 42 over McCourt et al. or Zhou et al.

Applicants' Response to the 35 U.S.C. 102(b)/103(a) Rejection of the Claims

In the Office Action, the Examiner rejected Applicants' claims 19-27 and 41-47 under 35 U.S.C. 102(b) as being anticipated by or, in the alternative,

under 35 U.S.C. 103(a) as obvious over Yannariello-Brown et al., Glycobiology 7:15. Applicants respectfully traverse the rejection of pending claims 24 and 42, as now amended, for the reasons stated herein below.

Applicants' pending claim 24 recites a purified mammalian HARE comprising a protein specifically able to bind HA, chondroitin and/or chondroitin sulfate and comprising a sequence essentially as set forth in SEQ ID NO:2. Applicants' pending claim 42 recites a purified composition comprising a functionally active HARE polypeptide having an amino acid sequence essentially as set forth in SEQ ID NO:2 or SEQ ID NO:25.

Yannariello-Brown et al. describe the identification of a 175 kDa protein in rat liver endothelial cells (LEC) that binds HA. LEC membrane extracts were separated by nonreducing SDS-PAGE and ligand blotted with ^{125}I-HA to identify HA-binding proteins, and a polypeptide having an M_r value of ~175,000 was identified. The extracts were also subjected to gel filtration chromatography, and fractions containing HA-binding activity were pooled to enrich the 175 kDa protein having HA-binding activity. However, this pool contained a large number of proteins that were not even clearly separable by SDS-PAGE (see Fig. 5B, S400 POOLS, lane 1). While the 175 kDa protein was "enriched" in this pool as compared with the LEC membrane extracts, the Yannariello-Brown et al. reference does not disclose the "isolation", and therefore the purification, of this protein, but rather only the "identification" thereof.

The purification of a mammalian HARE or a composition comprising a functionally active HARE polypeptide having a sequence essentially as set forth in SEQ ID NO:2 or SEQ ID NO:25 of the subject application would not be anticipated by nor obvious over the disclosure of the Yannariello-Brown et al. reference. Given the disclosure provided in the Yannariello-Brown et al. reference, a person having ordinary skill in the art would be required to perform a vast amount of unpredictable experimentation in attempting to purify a mammalian HARE or a composition comprising a functionally active HARE polypeptide comprising a sequence essentially as set forth in SEQ ID NO:2 or SEQ ID NO:25 without any instruction or guidance from the prior art, and therefore without any reasonable expectation of success. Such prior art suggestion for virtually endless experimentation alone necessitates a finding that the presently claimed invention is not obvious in light of *In re Dow Chemical Co.* (5 USPQ2d 1529, 1532 (Fed. Cir. 1989)).

At best, a person having ordinary skill in the art might be able to obtain a small fragment of amino acid sequence (at most 5-10 amino acids) by blotting the SDS-PAGE gel described in Yannariello-Brown et al. to a membrane, excising the desired ~175 kDa fragment and subjecting it to Edman sequencing. However, considering the number of proteins present in the SDS-PAGE gel of FIG. 5B of Yannariello-Brown et al., removal of a section of membrane that contains only the protein of interest would be virtually impossible. Further, even if this sequence were obtainable based on the

teachings of the Yannariello-Brown et al. reference, it would only be a small fragment of SEQ ID NO:2 or SEQ ID NO:25, without providing any guidance or instruction on purifying the entire protein and/or obtaining the rest of the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:25 without requiring a vast amount of undue experimentation. Due to the nature of the invention, the scope and content of the prior art and the level of unpredictability in the art, the present invention claimed in the subject application is not obvious over the Yannariello-Brown et al. reference.

Indeed, although the inventors worked diligently on purifying the mammalian HARE following submission of the Yannariello-Brown et al. reference, more than three years passed from the time the Yannariello-Brown et al. reference was submitted until the work describing the purification of the HARE was submitted (Zhou et al. reference) and the subject application was filed. Submitted herewith is a 37 CFR 1.132 declaration of co-Applicant Paul Weigel describing the difficulties that the Applicants encountered in purifying the mammalian HARE following publication of the Yannariello-Brown et al. reference that demonstrates the non-obviousness of the present invention, as recited in the claims of the subject application, over the Yannariello-Brown et al. reference.

In addition, other groups had attempted to identify and isolate the HARE but had been unsuccessful (see McCourt et al., Int. J. Biochem. Cell Biol. 29:1179-1189), thus further demonstrating the non-obviousness of the present

invention, as recited in the claims of the subject application.

Therefore, Applicants respectfully submit that claims 24 and 42, as now amended, are neither anticipated by nor obviousness over the Yannariello-Brown et al. reference. Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. 102(b)/103(a) rejection of pending claims 24 and 42 over Yannariello-Brown et al.

CONCLUSION

This is meant to be a complete response to the Office Action mailed August 16, 2002. Applicant respectfully submits that each and every rejection of pending claims 24 and 42, as now amended, has been overcome, and that such claims as well as newly added claim 88 are now in a condition for allowance. Further, Applicants respectfully request that upon allowance of generic claim 42 or 88, claim 28 be rejoined and considered. Favorable action is respectfully requested.

Should the Examiner have any questions or comments concerning the before-mentioned amendments to the application or any other matter, Applicant's agent will welcome the opportunity to discuss same with the Examiner.

Respectfully submitted,

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REDLINE VERSION OF THE CLAIMS

24. A purified mammalian HARE, comprising:

a protein which is able to specifically bind at least one of HA, chondroitin and chondroitin sulfate, the protein comprising a sequence **[in accordance with]** **essentially as set forth in** SEQ ID NO:2.

28. A purified mammalian HARE, comprising:

a protein which is able to specifically bind at least one of HA, chondroitin and chondroitin sulfate, the protein comprising a sequence **[in accordance with]** **essentially as set forth in** SEQ ID NO:25.

42. A purified composition, wherein the purified composition comprises a functionally active HARE polypeptide, wherein the functionally active HARE polypeptide has an amino acid sequence selected from the group consisting of an amino acid sequence **[in accordance with]** **essentially as set forth in** SEQ ID NO:2 and an amino acid sequence **[in accordance with]** **essentially as set forth in** SEQ ID NO:25.